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Ventilation by external high-frequency oscillations improves cardiac function after coronary artery bypass grafting[1]

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Abstract

Objective: To compare the effects of ventilation with intermittent positive pressure and external high frequency oscillation by the Hayek Oscillator during the first 5 h after coronary artery bypass grafting. *Methods:* Eleven patients were randomized to intermittent positive pressure ventilation throughout the observation period (5 h), while 13 patients were initially ventilated with intermittent positive pressure ventilation, then by external high-frequency oscillations for 4 h, changing to positive pressure ventilation for the last hour. *Results:* Cardiac index, stroke volume index, right ventricular stroke work index, right ventricular end-diastolic volume index and mixed venous oxygen saturation were significantly increased during ventilation with external high-frequency oscillations, and arteriovenous oxygen content difference was significantly reduced. There were no significant inter- or intragroup differences in fluid accumulation, mean arterial blood pressure, arterial blood gases, pulmonary artery pressure, central venous pressure, pulmonary capillary wedge pressure, heart rate, systemic vascular resistance index, pulmonary vascular resistance index, intrapulmonary shunt fraction, right ventricular ejection fraction, right ventricular end-systolic volume index and left ventricular stroke work index. *Conclusions:* Ventilation by external high-frequency oscillations increases cardiac index and improves tissue perfusion. The increased pumping of the heart is probably caused by changes of the intracardiac pressure–volume relationship. The Hayek Oscillator may have distinct cardiovascular benefits as ventilatory assistance in postoperative cardiac surgical patients. © 1997 Elsevier Science B.V.

Keywords: Coronary artery bypass grafting; Cuirass; External high-frequency oscillations; Positive pressure ventilation; Negative pressure ventilation; Postoperative; Ventilation

1. Introduction

Cyclic negative pressure ventilation (NPV), in use for more than 150 years [43,44], is based on creation of subatmospheric pressure inside a chamber in the inspiratory phase (creating active inspiration), while expiration is by passive recoil of the chest. NPV is provided either by a tank enclosing the body except for the neck [11], or by cuirass or cabinet ventilators, where the subatmospheric pressure is confined to the anterior chest and the upper abdomen.

The tank negative pressure ventilator, although capable of ventilating normal lungs, is less efficient in sick lungs with reduced lung volume and compliance. Haemodynamically, the tank negative pressure ventilator is no different to positive pressure ventilation (PPV), as it encloses the whole body [26]. The cuirass negative pressure ventilator may improve venous return, but it may increase afterload and at the same time cannot provide complete ventilation [26,35]. NPV by cuirass ventilators is reported to have a beneficial haemodynamic effect in dogs with oleic-acid-induced pulmonary oedema [37] and in pharmacologically induced left ventricular failure in dogs [38]. However, NPV increased extravascular lung water in a dog model with oleic-acid-induced pulmonary oedema [23].

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Nowadays NPV is seldom used, having ceded its place to PPV [26]. However, PPV may be a double-edged sword due to depression of cardiovascular function [35]. Depression of cardiac output (CO) with PPV has usually been attributed to diminished venous return [2,7,24,34], but has also been suggested to be caused by other mechanisms, such as ventricular interdependence [19,20], humoral cardiodepression [13,28], neural reflexes [5,6], or myocardial ischaemia [41].

Recently, a new method of ventilation, using a specially developed cuirass, has been introduced. This is the Hayek Oscillator which uses high frequency ventilation, most often between 60 and 90 cycles/min. Both the inspiratory and the expiratory phases are active. The chest is oscillated around a variable negative mean pressure. Consequently, its way of functioning has been described as external high frequency oscillation (EHFO) around a negative baseline [9,10,15–17,40]. Ventilation with the Hayek Oscillator significantly increases pulmonary blood flow as compared with intermittent positive pressure ventilation (IPPV) after the Fontan operation [29,30]. Smithline et al. [39] showed that the Hayek Oscillator used in conjunction with IPPV may increase cardiac output and coronary blood flow during cardiopulmonary resuscitation. In addition, use of the advanced cuirass EHFO provides adequate ventilation for both normal and sick lungs in both paralysed and spontaneously breathing patients [9,10,15,40]. The active expiratory and inspiratory phases allow ventilation at high frequencies, creating positive airway pressure during expiration, increasing lung volume, and avoiding excessive negative thoracic pressure otherwise needed to improve lung volume in conventional NPV [17].

The purpose of the present study was to compare the effect of IPPV with EHFO around a negative baseline, using the Hayek Oscillator, on pulmonary and cardiovascular function in the immediate postoperative course after elective coronary artery bypass grafting. In addition to comparing one group of patients receiving EHFO with another group receiving IPPV, the patients in the EHFO group were their own controls: we investigate what happens when EHFO are instituted after control measurements on the respirator, and what happens when this process is reversed.

2. Materials and methods

The study was approved by the Ethics Committee of the Karolinska Hospital, and carried out in accordance with the guidelines of the hospital for studies of this nature. Informed consent was obtained from each patient. The patient characteristics and the criteria for inclusion or exclusion in the study are listed in Tables 1 and 2.

Table 1
Inclusion and exclusion criteria for patients randomized to either IPPV or EHFO in the immediate postoperative course after coronary artery bypass grafting

Inclusion criteria	
Sex	Male
Age	55–80 years
Operation	Elective coronary artery bypass grafting, 3–5 distal anastomoses
Left ventricular function	No history of cardiac failure; CI > 1.5 l/m^2 at the baseline postoperative measurement
Cardiac rhythm	Sinus rhythm
Renal function	Serum creatinine < 120 μmol/l
Exclusion criteria	
Diabetes	Insulin dependent
Pulmonary disease	Obstructive and restrictive disease in need of regular medication
Peroperative problems	Difficult to wean off bypass; use of inotropic drugs
Postoperative	Inotropic support; reoperation or bleeding > 1000 ml during the observation period; arrhythmias; perioperative myocardial infarction
Miscellaneous	Pacemaker

2.1. Anaesthesia, recording of haemodynamics, and operative procedures

Anaesthesia was induced and maintained with midazolam and fentanyl, and muscle relaxation with pancuronium. Arterial pressure was monitored via a radial artery line. A balloon-tipped pulmonary artery catheter (Edwards, Swan Ganz Right Ventricular Ejection Fraction catheter, 93A-434H-7.5F, Baxter) was introduced via the right external jugular vein for measurement of cardiac output (CO), pulmonary arterial pressures (PAP), pulmonary capillary wedge pressure (PCWP) and right ventricular volumes. CO and right ventricular volumes were measured by thermodilution, using ice-cold injectate, and employing an Edwards REF-1 Ejection Fraction Cardiac Output monitor (Baxter). For each measurement of CO, five injections were per-

Table 2
Patient data and characteristics

Characteristic	IPPV	EHFO
Age (years)	68 ± 6	63 ± 4
Height (cm)	177 ± 4	176 ± 7
Weight (kg)	87 ± 9	83 ± 8
Time on bypass (min)	77 ± 19	84 ± 27
Aortic cross-clamp (min)	40 ± 11	46 ± 19
Distal anastomoses	3.8 ± 0.8	3.8 ± 1.2

Patients were randomized to either IPPV ($n = 11$) or EHFO ($n = 13$) in the immediate postoperative course after coronary artery bypass grafting. All data are mean ± S.D.

formed, the highest and lowest reading were discarded, and the mean of the remaining three accepted as the measured CO. Concurrent with drawing systemic arterial blood, blood was sampled through the pulmonary artery catheter for measurement of blood gases in mixed venous blood (ABL 505, Radiometer, Copenhagen), including direct measurements of oxygen saturation for calculations of arteriovenous oxygen content differences ($A-V_{O_2diff}$). Intrapulmonary shunt fraction (Q_S/Q_T) was calculated by the following formula:

$$Q_S/Q_T = C_{cO_2} - C_{aO_2}/C_{cO_2} - C_{vO_2}$$

where C_{cO_2} is oxygen content in pulmonary capillary blood; C_{aO_2} is oxygen content in arterial blood; C_{vO_2} is oxygen content in mixed venous blood [26]. C_{cO_2} was calculated by the following formula: $C_{cO_2} =$ (Haemoglobin $\times$ 1.39) $\times$ alveolar oxygen saturation + ($P_{aO_2} \times 0.0031$) [26].

Heparin was given to achieve an activated clotting time over of 480 s. A standard aortic and a two-stage venous cannula were used. A Maxima membrane oxygenator was used in the extracorporeal circuit, which was primed with Ringer acetate. Cardiopulmonary bypass (CPB) was conducted at a minimum temperature in venous blood of 31 ± 2°C (mean $\pm$ S.D.) with non-pulsatile flow (1.8 l/min per m^2, blood pressure above 40 mmHg). Cardioplegic arrest was induced by antegrade infusion of cold (4–6°C) St. Thomas' II solution (700–900 ml). Repeated cardioplegic infusions (200–300 ml) were given each 15–20 min during aortic cross-clamping, either antegradely or retrogradely via a self-inflating coronary sinus catheter (Research Medical). Upon completion of the distal anastomoses, the aortic cross-clamp was released, and the proximal anastomoses were performed with a side-biting clamp on the ascending aorta. The left internal mammary artery was used for revascularization in every patient. Rewarming was started 10 min before release of the cross-clamp. When the patients were weaned off CPB, body temperature was over 36°C, and the heparin effect was reversed by protamine chloride.

2.2. Experimental protocol

In the intensive care unit, all patients were stabilized on IPPV before baseline measurements of haemodynamics and blood gases were performed approximately 45 min after arrival (= 0 h, H0), after which they were randomized to ventilation with either the Hayek Oscillator (Flexco Medical Instruments AG, Zürich, Switzerland) (EHFO group, $n = 14$) or IPPV (IPPV group, $n = 14$). In the cuirass group, one patient was excluded during the study due to a perioperative septal infarction after endartherectomy of the left anterior descending artery (LAD). In the IPPV group, two patients were excluded due to failure of the Swan Ganz catheter and inadequate haemodynamic monitoring. A third patient was excluded because of reoperation due to bleeding during the observation time. Consequently, 11 patients with IPPV and 13 patients with EHFO finished the study. Complete measurements of haemodynamics and blood gases were repeated after 1, 2, 3 and 4 h (H1, H2, H3 and H4). After the measurement at 4 h, the EHFO group changed back to IPPV, and a final measurement was done after 5 h (H5), when the patients in both groups were on IPPV. All patients were sedated by propofol, 8 mg/kg per h.

2.3. Ventilation

Throughout the study, inspiratory gases were kept at room temperature. The blood values of pH and P_{CO_2} were not corrected for actual body temperature.

2.3.1. IPPV

Upon arrival in the intensive care unit, the respirator (Erica Engström) was adjusted by the anaesthesiologist to settings that were clinically judged as favourable according to the pre- and peroperative respiratory behaviour of that particular patient, and to the standard employed for routine cases in our clinic. During the observation period, changes in the respirator setting were kept at an absolute minimum, and F_{iO_2} maintained at 0.40. IPPV settings were as follows: frequency 17 ± 2 breaths/min; tidal volume 0.52 ± 0.08 l; end-expiratory pressure 0, and inspiratory–expiratory ratio 1:2.

2.3.2. EHFO

The Hayek Oscillator cuirass is a flexible, lightweight plastic shell that covers the anterior part of the chest and upper abdomen, having foam skirt edges which create an airtight seal. It has a backplate and is secured by Velcro straps [9,15,17,40]. The cuirass is connected by wide-bore flexible tubings to the mobile, microprocessor-controlled power unit. Within the power unit is a diaphragmatic pump that operates over a wide range of frequencies, 8–999 cycles per min. The frequency, inspiratory and expiratory pressure in the cuirass chamber, and inspiratory–expiratory (I:E) ratio can be set at the automatic control unit, which then adjusts the performance by negative feedback from a pressure transducer [9,10,17].

The settings of the Hayek Oscillator were chosen empirically from what would be expected to be adequate ventilation with EHFO in other conditions [9,10,15,40]. The initial setting was changed if arterial blood gases within 20 min indicated that ventilation ought to be improved, after which the EHFO ventilation remained unchanged throughout the period of observation. The settings were as follows: frequency 72 cycles/min; end-inspiratory chamber pressure -29 ± 6 cmH_2O; end-expiratory chamber pressure 3 ± 5

cmH_2O, *I*:*E* ratio 1:1. When using the Hayek Oscillator without use of a pneumotachograph, it is only possible to obtain approximate readings of tidal volume. Minute ventilation is therefore not included in the present report. F_{iO_2} was 0.40 during ventilation with EHFO. After 4 h, EHFO was replaced by IPPV with the following settings: frequency 17 breaths/min, tidal volume 0.5 l, end-expiratory pressure 0, *I*:*E* ratio 1:2, and F_{iO_2} 0.40.

2.4. Statistical methods

For statistical evaluation, professional assistance was obtained (Elisabeth Berg, Department of Medical Informatics and Educational Development, Karolinska Institute, Stockholm). The data were analyzed according to a repeated measures analysis of variance (ANOVA) with one independent and one dependent factor. The independent factor is treatment with levels 'EHFO' and 'IPPV' and the dependent factor is time with the levels ' 0, *x*, . . . and 5 h' (H0, H1, + . . . H2, and H5). When the over all *F*-ratio in the ANOVA was significant at the 5% level, contrast between the repeated measures was calculated. In case of a significant interaction between treatment and time, simple main effects were examined, i.e. effects of one factor holding the other factor fixed [21]. We specifically wanted to see if change from IPPV to EHFO within the group had an effect (H0 versus H1 + . . . H4), if treatment with EHFO was different from IPPV (comparing the compact H1 + . . . H4 in the two groups), and also to investigate if changing from EHFO to IPPV within the group had any effect (H1 + . . . H4 versus H5). Due to within-subject correlations amongst the repeated measurements, *P*-values have been adjusted according to Greenhouse–Geisser (GG) [21]. *P*-values and GG < 0.05 are regarded as significant. Data in text and tables are presented as mean ± S.D., and in the figures as mean ± 95% confidence interval.

3. Results

3.1. Clinical course

At the end of CPB, the patients to be included in the IPPV group were estimated to have accumulated 2.9 ± 0.6 l fluid, not including perspiration in the fluid balance. At the end of the observation period, this was unchanged (2.9 ± 0.8 l). Fluid accumulation in the EHFO group was 2.3 ± 1.0 l and 2.7 ± 1.1 l, respectively. There were no significant inter- or intragroup differences. No patient needed inotropic support. All patients were weaned off respirator and extubated within 12 h, and they were all transferred from the intensive care unit to a regular ward on the 1st postoperative day. The further postoperative course was uneventful for all patients. There were no perioperative myocardial infarctions as judged by myocardial enzymes and electrocardiograms.

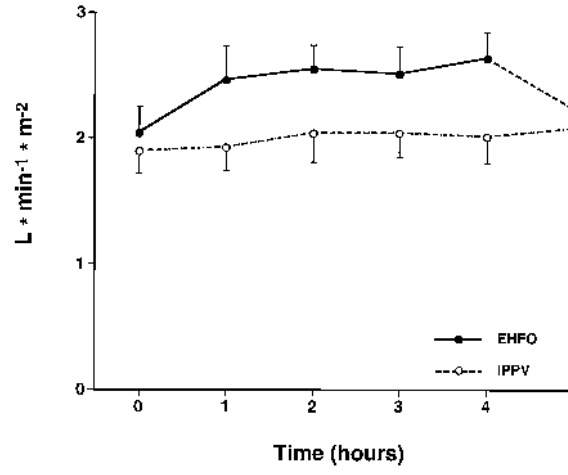

Fig. 1. Cardiac index (CI) in two groups of patients after coronary artery bypass grafting. One group ($n = 11$) is ventilated with IPPV, the other group ($n = 13$) is ventilated with EHFO by the Hayek Oscillator. The time 0 h represents baseline measurements on IPPV 45 min after arrival in the intensive care unit, after which the patients were randomized to either the IPPV or EHFO group. After 4 h, the patients in the EHFO group changed to IPPV. All values are mean ± 95% confidence interval. CI is significantly increased in the EHFO group (see text for details on statistics).

3.2. Cardiac index

Before randomization, cardiac index (CI; Fig. 1) was 1.9 ± 0.18 and 2.0 ± 0.24 l/min per m^2 in the IPPV and the EHFO groups, respectively. In the EHFO group, CI was increased after 1 h (2.4 ± 0.26 l/min per m^2), reaching a maximum of 2.6 ± 0.20 l/min per m^2 after 4 h. Changing from IPPV to EHFO increased CI ($P < 0.0001$, GG < 0.0001), and during treatment, CI remained higher in the EHFO group compared with IPPV ($P < 0.004$). After 4 h when EHFO changed to IPPV, CI decreased ($P < 0.0001$, GG < 0.002) at 5 h.

3.3. Mixed venous saturation

Baseline mixed venous saturation (S_{vO_2}; Fig. 2) was 63 ± 3 and 64 ± 4% in IPPV and EHFO groups, respectively. In the IPPV group, S_{vO_2} gradually decreased during the observation period with a minimum after 4 h (59 ± 4%). After start of EHFO treatment, S_{vO_2} increased ($P < 0.0002$, GG < 0.003), remained higher than in the IPPV group during treatment ($P < 0.001$), reached a maximum of 70 ± 3% after 4 h, but decreased to 66 ± 3% at 5 h when EHFO had been replaced by IPPV ($P < 0.004$, GG < 0.02).

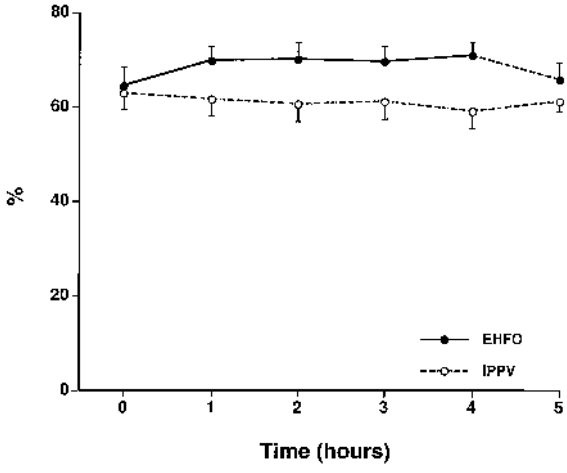

Fig. 2. Mixed venous saturation (S_{vO_2}) in two groups of patients after coronary artery bypass grafting. One group ($n = 11$) is ventilated with IPPV, the other group ($n = 13$) is ventilated with EHFO by the Hayek Oscillator. The time 0 h represents baseline measurements on IPPV 45 min after arrival in the intensive care unit, after which the patients were randomized to either the IPPV or EHFO group. After 4 h, the patients in the EHFO group changed to IPPV. All values are mean $\pm$ 95% confidence interval. S_{vO_2} was significantly increased in the EHFO group (see text for details on statistics).

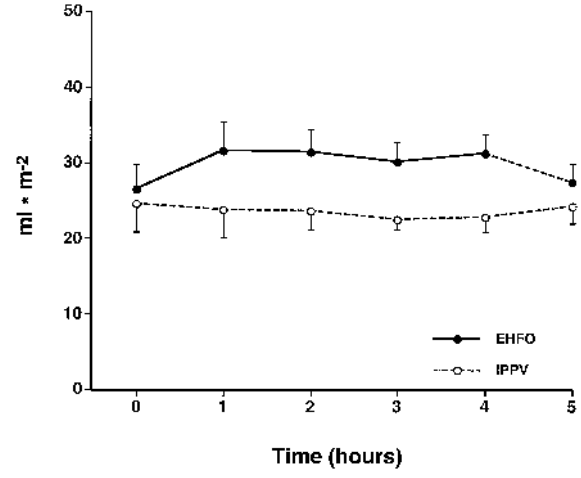

Fig. 4. Stroke volume index (SVI) in two groups of patients after coronary artery bypass grafting. One group ($n = 11$) is ventilated with IPPV, the other group ($n = 13$) is ventilated with EHFO by the Hayek Oscillator. The time 0 h represents baseline measurements on IPPV 45 min after arrival in the intensive care unit, after which the patients were randomized to either the IPPV or EHFO group. After 4 h, the patients in the EHFO group changed to IPPV. All values are mean $\pm$ 95% confidence interval. SVI is significantly increased in the EHFO group (see text for details on statistics).

3.4. Arteriovenous oxygen content difference

The baseline arteriovenous oxygen content difference ($A-V_{O_2diff}$; Fig. 3) at 0 h was 51 ± 5 and 55 ± 7 ml/l in the IPPV and EHFO groups, respectively. In the EHFO group, $A-V_{O_2diff}$ decreased after the start of treatment ($P < 0.0001$, GG < 0.001), reaching a minimum (43 ± 3 ml/l) after 4 h. The $A-V_{O_2diff}$ was lower than in the IPPV group during treatment ($P < 0.0002$), but increased when IPPV replaced EHFO (51 ± 4 ml/l at 5 h) ($P < 0.003$, GG < 0.01). In the IPPV group, $A-V_{O_2diff}$ increased during the observation period ($P < 0.002$).

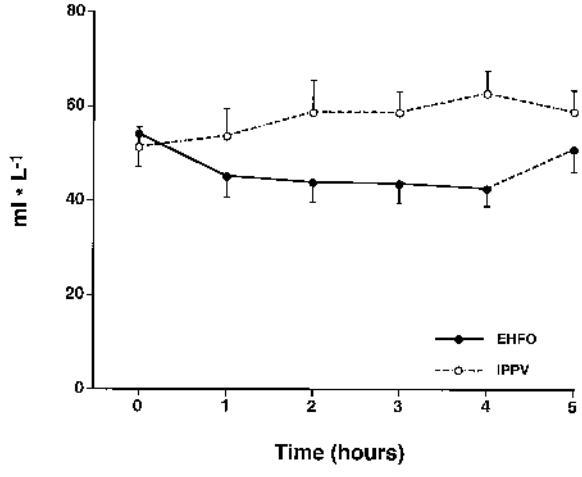

Fig. 3. Arteriovenous oxygen content difference ($A-V_{O_2diff}$) in two groups of patients after coronary artery bypass grafting. One group ($n = 11$) is ventilated with IPPV, the other group ($n = 13$) is ventilated with EHFO by the Hayek Oscillator. The time 0 h represents baseline measurements on IPPV 45 min after arrival in the intensive care unit, after which the patients were randomized to either the IPPV or EHFO group. After 4 h, the patients in the EHFO group were changed back to IPPV. All values are mean $\pm$ 95% confidence interval. $A-V_{O_2diff}$ is significantly decreased in the EHFO group (see text for details on statistics).

3.5. Stroke volume index

Stroke volume index (SVI; Fig. 4) was initially 25 ± 3.6 and 26 ± 3.2 ml/m^2 in IPPV and EHFO groups, respectively. SVI increased after the start of EHFO treatment ($P < 0.0001$, GG < 0.0004), remained significantly higher than in the IPPV group during treatment ($P < 0.01$), and decreased when IPPV replaced EHFO ($P < 0.0004$, GG < 0.004).

3.6. Right ventricular end-diastolic volume index

There was no difference in right ventricular end-diastolic volume index (RVEDVI; ml/m^2; Fig. 5) in the basal situation (H0) between EHFO and IPPV group. When EHFO was instituted, RVEDVI increased ($P < 0.002$, GG < 0.02), remained higher during treatment than in the IPPV group ($P < 0.03$), but did not decrease significantly when IPPV replaced EHFO.

3.7. Miscellaneous haemodynamics (Table 3)

Mean arterial blood pressure, systolic and diastolic pulmonary artery pressure, central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP), heart rate, systemic vascular resistance index (SVRI), left ventricular stroke work index, right ventricular end-systolic volume index, right ventricular stroke work index, pulmonary vascular resistance index (PVRI), intrapulmonary shunt fraction and right ventricular ejection fraction in the IPPV and the EHFO groups are presented in Table 3. Right and left ventricular stroke work index were significantly increased by EHFO (Table 3). No other inter- or intragroup differences were found, although SVRI remained constantly lower during EHFO treatment. It is noteworthy that filling pressures of both the right and the left ventricle (CVP and PCWP) were similar in the two groups.

3.8. Temperatures, blood gases, haemoglobin and haematocrit

Blood and rectal temperatures as well as blood gases are shown in Table 4. The baseline postoperative values were similar in the two groups. Although not statistically significant, the EHFO patients had lower temperatures, higher P_{CO_2}, and lower pH during the first postoperative hours (Table 4). In the IPPV and EHFO groups, haemoglobin was initially 109 ± 11 and 117 ± 10 g/l, and after 5 h, 115 ± 7 and 113 ± 12 g/l, respectively. Haematocrit was not different in the two groups (basal value $34 \pm 3\%$ (IPPV group) and $36 \pm 3\%$ (EHFO group); after 5 h, $35 \pm 2\%$ in both groups).

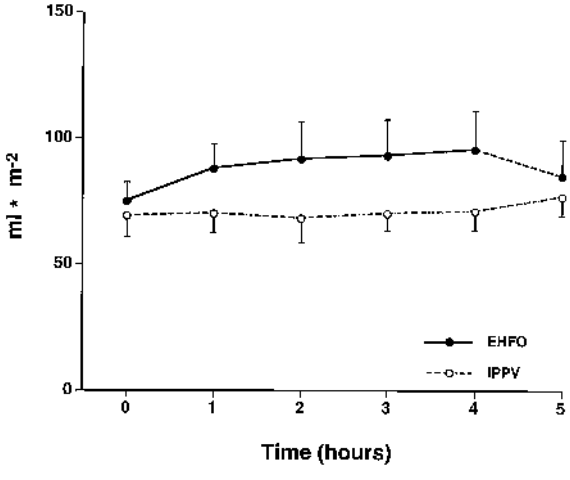

Fig. 5. Right ventricular end-diastolic volume index (RVEDVI) in two groups of patients after coronary artery bypass grafting. One group ($n = 11$) is ventilated with IPPV, the other group ($n = 13$) is ventilated with EHFO by the Hayek Oscillator. The time 0 h represents baseline measurements on IPPV 45 min after arrival in the intensive care unit, after which the patients were randomized to either the IPPV or EHFO group. After 4 h, the patients in the EHFO group changed to IPPV. All values are mean $\pm$ 95% confidence interval. RVEDVI is significantly increased in the EHFO group (see text for details on statistics).

4. Discussion

There are several distinct differences in the response to ventilation between the EHFO group and the IPPV group. In the EHFO group, CI and mixed venous oxygen saturation increased significantly, while $A-V_{O_2diff}$ decreased, indicating improved perfusion and oxygenation of peripheral tissues. There was no significant difference in mean arterial blood pressure or SVRI between the two groups. These findings strongly suggest that increased CI and tissue perfusion were primarily caused by increased pumping of the heart, and not due to peripheral vasodilatation. However, in previous studies using EHFO, both increased cardiac output [29,30] as well as no cardiovascular difference in comparison to CPPV were found [1,3].

The present study does not provide insight into the mechanisms of the observed differences, which can only be the object of speculation. The main mechanistic difference that separates the Hayek Oscillator from 'conventional' NPV by cuirass is that the Hayek Oscillator operates at high frequencies, employs active expiration, and both peak inspiratory chamber pressure and end-expiratory chamber pressure are controllable [9,10,15–17,40]. The end-expiratory chamber pressure can be set at positive, zero, or negative. It has been speculated that end-expiratory chamber pressure is an indirect positive end expiratory pressure (PEEP) which can be manipulated by changing the $I{:}E$ ratio, and increased by increasing the frequency [17]. However, no solid data exist regarding intrathoracic pressures during EHFO, and their relationship to $I{:}E$ ratio and end-expiratory chamber pressure. Findings with continuous NPV cannot automatically be valid for EHFO.

A negative pressure during the respiratory cycle does not necessarily have the opposite cardiovascular effects of IPPV. A decrease in mean intrathoracic pressure will influence both venous return and ventricular afterload [35]. The generation of more negative intrathoracic pressure will increase venous return until a specific maximum flow rate is reached [14]. A decrease in right ventricular preload is the clinically most important mechanism of the decrease in right ventricular stroke volume during PPV [25]. In the present work, there was no effect on right ventricular afterload. However, although the filling pressure (CVP) was similar in both groups, right ventricular end-diastolic volume was higher when using EHFO, probably because lower mean intrathoracic pressure with EHFO may reduce the juxtacardiac pressures, thus increasing the transmural distending pressure. The lack of correlation between

Table 3
Haemodynamic data in patients treated with either IPPV ($n = 11$) or EHFO ($n = 13$) after coronary artery bypass grafting

Measured	Group	0 h	1 h	2 h	3 h	4 h	5 h
MAP (mmHg)	IPPV	83 ± 17	80 ± 13	86 ± 12	79 ± 12	76 ± 9	80 ± 9
	EHFO	83 ± 16	86 ± 13	83 ± 11	83 ± 11	83 ± 11	87 ± 15
PAP_{syst} (mmHg)	IPPV	25 ± 9	24 ± 6	26 ± 6	26 ± 6	26 ± 5	27 ± 5
	EFHO	25 ± 7	30 ± 8	29 ± 6	31 ± 9	34 ± 9	26 ± 9
PAP_{diast} (mmHg)	IPPV	13 ± 4	14 ± 4	15 ± 5	15 ± 6	13 ± 3	14 ± 3
	EHFO	12 ± 4	12 ± 7	12 ± 5	11 ± 6	14 ± 5	14 ± 6
CVP (mmHg)	IPPV	7 ± 4	6 ± 4	8 ± 4	7 ± 4	7 ± 3	8 ± 2
	EHFO	7 ± 3	6 ± 4	6 ± 4	7 ± 4	8 ± 3	9 ± 4
PCWP (mmHg)	IPPV	8 ± 4	8 ± 5	8 ± 5	8 ± 4	8 ± 3	8 ± 3
	EHFO	7 ± 3	8 ± 4	9 ± 4	9 ± 3	9 ± 2	5 ± 1
Heart rate (per min)	IPPV	80 ± 12	83 ± 13	87 ± 10	90 ± 14	88 ± 16	88 ± 14
	EHFO	79 ± 14	81 ± 15	83 ± 13	83 ± 13	84 ± 12	82 ± 10
SVRI ($\times 10^3$) (dyne/s per cm^5 per m^2)	IPPV	3.33 ± 1.15	3.17 ± 0.86	3.17 ± 0.74	2.95 ± 0.75	2.88 ± 0.74	2.87 ± 0.62
	EHFO	3.23 ± 1.03	2.75 ± 0.59	2.48 ± 0.49	2.54 ± 0.63	2.36 ± 0.56	2.85 ± 0.59
LVSWI[a] (gm/m^2)	IPPV	24 ± 6.0	22.6 ± 6.5	24.8 ± 5.8	21.7 ± 4.6	21.2 ± 3.6	23.4 ± 4.6
	EHFO	26.9 ± 9.4	34.1 ± 9.1	32.0 ± 8.2	30.3 ± 6.1	31.5 ± 6.4	29.2 ± 6.9
PVRI (dyne/s per cm^5 per m^2)	IPPV	426 ± 151	414 ± 154	438 ± 131	428 ± 152	446 ± 102	429 ± 126
	EHFO	436 ± 198	401 ± 203	325 ± 132	361 ± 182	422 ± 191	3210 ± 192
Q_S/Q_T (%)	IPPV	33 ± 7	29 ± 6	27 ± 7	26 ± 3	26 ± 9	27 ± 4
	EHFO	28 ± 9	30 ± 7	32 ± 4	32 ± 4	30 ± 11	28 ± 5
RVESVI (ml/m^2)	IPPV	44 ± 10	46 ± 11	45 ± 15	47 ± 13	48 ± 14	53 ± 14
	EHFO	50 ± 14	59 ± 19	62 ± 24	65 ± 23	66 ± 24	59 ± 23
RVSWI[b] (gm/m^2)	IPPV	3.5 ± 1.6	3.7 ± 1.3	3.6 ± 1.4	3.6 ± 0.8	3.4 ± 0.9	3.6 ± 0.9
	EHFO	3.8 ± 1.8	5.4 ± 1.9	5.7 ± 2.2	5.7 ± 2.4	6.1 ± 2.2	3.8 ± 2.5
RVEF (%)	IPPV	36 ± 7	34 ± 7	36 ± 7	33 ± 7	33 ± 7	32 ± 7
	EHFO	34 ± 10	36 ± 12	35 ± 9	33 ± 9	33 ± 9	33 ± 9

MAP, mean arterial blood pressure; PAP_{syst}/PAP_{diast}, systolic and diastolic pulmonary arterial pressure; CVP, central venous pressure; PCWP, pulmonary capillary wedge pressure; SVRI, systemic vascular resistance index; LVSWI, left ventricular stroke work index; PVRI, pulmonary vascular resistance index; Q_S/Q_T, intrapulmonary shunt fraction; RVESVI, right ventricular end-systolic volume index; RVEDVI, right ventricular end-diastolic volume index; RVSWI, right ventricular stroke work index; RVEF, right ventricular ejection fraction; gm, gram-meter. The time 0 h represents baseline measurements on IPPV 45 min after arrival in the intensive care unit, after which the patients were randomized to either the IPPV or EHFO group. After 4 h, the patients in the EHFO group changed to IPPV. All values are mean ± S.D.

[a] LVSWI was increased by EHFO ($P < 0.003$, GG < 0.02), remained higher during treatment with EHFO ($P < 0.001$), but did not decrease when IPPV replaced EHFO.

[b] RVSWI increased when EHFO started ($P < 0.002$, GG < 0.006), remained higher than the IPPV group during EHFO, and decreased when IPPV replaced EHFO ($P < 0.005$, GG < 0.02).

right ventricular filling pressure and end-diastolic volume as well as the role of pericardial pressure in the right ventricular pressure–volume relationship has recently been investigated after cardiac surgery [31]. Unfortunately, no volume data of the left ventricle are available in the present study. However, a decrease in mean intrathoracic pressure requires the left ventricle to generate greater transmural pressures, thereby increasing afterload. Increased transmural pressure may increase left ventricular preload by increasing end-diastolic volume at the same filling pressure. Theoretically, increased volume of the right ventricle may cause leftward displacement of the interventricular septum and decreased left ventricular compliance [4]. Thus, changes that will both increase and decrease CI probably occur concurrently during NPV. In EHFO, the active expiratory phase may, compared with conventional NPV, partly prevent increased afterload.

Stroke volume index, and both right and left ventricular stroke work index, tended to be higher in the EHFO group. Using EHFO may be equivalent to moving to a higher ventricular volume at the same pressure, thus creating a new Frank Starling curve with new pressure–volume relationships of the ventricles. This may theoretically be the mechanism of increased CI by EHFO. The concurrent increase in ventricular work load and afterload may not influence cardiac function and overall pumping efficiency at the afterload level in the present study situation.

Table 4
Temperatures and blood gases

Measured	Group	0 h	1 h	2 h	3 h	4 h	5 h
Blood temp. (°C)	IPPV	36 ± 0.9	36.1 ± 1	36.7 ± 1.2	37.2 ± 1.2	37.6 ± 1.2	37.8 ± 1.2
	EHFO	35.9 ± 0.7	35.9 ± 0.7	36.3 ± 0.5	36.6 ± 0.7	36.8 ± 0.7	37.2 ± 0.7
P_{aO_2} (kPa)	IPPV	11.6 ± 3.3	13.0 ± 3.9	13.4 ± 3.4	13.1 ± 2.1	13.3 ± 3.1	12.9 ± 3.0
	EHFO	14.7 ± 6.5	12.5 ± 3.8	13.1 ± 3.5	13.1 ± 4.1	12.7 ± 2.8	12.8 ± 3.4
pH	IPPV	7.42 ± 0.07	7.43 ± 0.08	7.43 ± 0.07	7.42 ± 0.05	7.42 ± 0.04	7.42 ± 0.05
	EHFO	7.41 ± 0.04	7.41 ± 0.10	7.38 ± 0.11	7.38 ± 0.11	7.37 ± 0.09	7.42 ± 0.06
Base excess (mekv/l)	IPPV	−0.1 ± 2.1	−0.4 ± 2.1	−0.2 ± 1.8	−0.1 ± 1.2	−0.0 ± 1.1	0.4 ± 1.4
	EHFO	−0.8 ± 1.0	−0.5 ± 1.3	−0.7 ± 1.2	−0.6 ± 1.5	−0.7 ± 1.4	0.3 ± 1.6
P_{aCO_2} (kPa)	IPPV	4.9 ± 0.5	4.8 ± 1.0	4.8 ± 0.9	5.0 ± 0.8	5.1 ± 0.7	4.9 ± 0.5
	EHFO	5.1 ± 0.6	5.4 ± 1.6	6.0 ± 1.8	5.7 ± 1.8	6.0 ± 1.6	5.1 ± 0.8

Blood temperature (temp.) measured inn the pulmonary artery by a Swan Ganz catheter, and blood gases (not corrected for actual body temperature) in patients treated with either IPPV ($n = 11$) or EHFO ($n = 13$) after coronary artery bypass grafting. The time 0 h represents baseline measurements on IPPV 45 min after arrival in the intensive care unit, after which the patients were randomized to either the IPPV or EHFO group. After 4 h, the patients in the EHFO group changed to IPPV. All values are mean ± S.D. There was no inter- or intragroup difference.

Increased carbon dioxide in blood may increase cardiac output and decrease systemic vascular resistance [8,33]. Consequently, the increased P_{CO_2} in the EHFO group may theoretically contribute to the observed haemodynamic improvements, but several factors suggest that CO_2-induced changes in haemodynamics are not likely to be the most important explanation. In particular, increases in P_{CO_2} which are seen to have significant haemodynamic consequences will also increase mean arterial blood pressure and heart rate significantly [8], and these parameters did not change in the present study.

An interesting question is if the cardiovascular effects of EHFO are the same in patients with normal hearts and in patients with compromised heart function. In our patients, there were no clinical signs of heart failure. However, postcardioplegic hearts are not normal, since temporary postoperative reduction in cardiac function is a regular finding after open-heart surgery [22]. During the time of observation, CI was generally low compared with normal values, and low CI explains the high values of PVRI and SVRI. Even in this group of uncomplicated postoperative patients, increased CI must be considered beneficial. The tendency towards lower SVRI in the EHFO group is most probably secondary to the increase in CI in this group.

The EHFO settings (frequency, inspiratory–expiratory ratio, cuirass chamber pressures) used in this study were in accordance with those previously found acceptable in the use of EHFO in other conditions [1,9,10,15–17,29,30,40], as well as during our preliminary tests. However, those settings may not necessarily have been the best ones. No attempt was made in the present study to test various settings of the Hayek Oscillator. The cardiovascular effects of EHFO probably depend on the pulmonary and cardiovascular status of the patient as well as on cuirass pressure, frequency and inspiratory–expiratory ratio, all of which will determine the lung volume and oscillating tidal volume at which ventilation is performed. Considerations when determining the setting of the cuirass in patients with acute or chronic lung problems, or cardiovascular dysfunction, may be totally different. For instance, patients with 'stiff' lungs will probably require totally different settings than a patient with normal lungs. In a study on normal subjects, significant intersubject variations in gas exchange was found independently of height and weight of the subjects [15]. Consequently, further studies to determine the best EHFO setting in various subgroups of patients may improve our results even more. Surprisingly, EHFO had no significant effect on PVR and intrapulmonary shunt fraction.

Another important question in the present study is whether the respirator settings and the mode of PPV used is the optimal one for this particular group of patients. We employed the 'normal' settings of IPPV used routinely after open-heart surgery in our institution, although this differs from some guidelines [36] which recommend larger tidal volumes (12–15 ml/kg) and slower ventilator rates (8–12/min) in order to compensate for the increased dead space and to counteract the development of atelectasis and auto-PEEP. In the present study with the higher ventilator rate employed, end-expiratory pressure was set to be zero. In addition, patients with pulmonary disease were excluded.

Ventilation at higher than conventional frequencies may supposedly influence the intrathoracic pressures, and thus, in theory, venous return and general haemodynamics. EHFO with 72 breaths/min might in some ways be compared with high-frequency jet ventilation, which may be less likely than conventional respirator

treatment to cause haemodynamic dysfunction [42], in particular in situations with already compromised haemodynamics [12,27]. Reports of the use of high-frequency jet ventilation in conjunction with cardiac surgery are extremely scarce. In one study in dogs, high-frequency jet ventilation impaired cardiovascular function significantly less than 'normal' respirator treatment after CPB and global myocardial ischaemia [18]. The investigators claimed that improved haemodynamics were caused partly by larger left ventricular volume and partly by improved left ventricular contractility. However, in a study on postoperative cardiac surgical patients, IPPV and high-frequency jet ventilation did not differ in their effects on CI and cerebral blood flow [32]. Since the present study is the first one of its kind, we decided to compare EHFO with our routine IPPV treatment as a starting point. Consequently, the relative contributions of negative pressure ventilation and high-frequency ventilation are not elucidated by the present investigation.

The Hayek cuirass itself is easy to employ and can even be used in awake patients without endotracheal intubation [15]. In the immediate postoperative period, it is necessary to have a respirator in close stand-by in case of urgent reoperations, since the cuirass must be removed to get access to the chest. We have observed no complications due to the cuirass itself either in this study or in general.

Postoperative low CI is a major cause of postoperative morbidity and mortality after open-heart surgery [22]. EHFO, as carried out with the Hayek Oscillator, provided adequate ventilation while improving CI and peripheral perfusion in a group of patients with uncomplicated postoperative course after coronary artery bypass grafting. This study is preliminary, but except for paediatric surgical patients [29,30], we are not aware of any other study with extensive haemodynamic monitoring in postoperative patients using the Hayek cuirass. The haemodynamic consequences of EHFO in comparison to IPPV are probably complex, depending on cuirass settings, intrathoracic pressures, pulmonary and myocardial function, as well as intravascular volume and filling. The postoperative course of all patients included in the study was uneventful. Consequently, we have obtained no information about the haemodynamic and outcome effects of EHFO in more complicated subgroups of patients. We cannot tell whether the haemodynamic improvements observed in the EHFO group can contribute significantly to the outcome in subgroups of patients. However, it appears reasonable to investigate more closely the physiology of ventilation with EHFO as well as the cardiovascular effects of EHFO in postoperative and critically ill patients. Studies over a longer period of time and in larger groups of patients are necessary to elucidate the possible clinical role of EHFO, which may have distinct benefits as ventilatory assistance in patients with low output after cardiac surgery.

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